CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

64164

CHEMISTRY REVIEW(S)

AADA APPROVAL SUMMARY

AADAs: 64-155, 64-164, 64-165, 64-166

DRUG PRODUCT: Cefaclor for Oral Suspension USP

FIRM: Ranbaxy Pharmaceuticals Inc.

DOSAGE FORM: Dry mixture for oral suspension

STRENGTH: 125 mg/5 mL, 187 mg/5 mL, 250 mg/5 mL, 375 mg/5 mL

CGMP STATEMENT/EIR UPDATE STATUS: Signed cGMP certifications were provided in the original submissions (section IX). The EER was found acceptable 8/5/97.

BIO STUDY: The bio study conducted on the 375 mg/5 mL strength was found acceptable by the Division of Bioequivalence, and waiver requests for the other strengths were granted 5/13/96.

METHOD VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S): The drug substance and drug product are both USP. The applicant is using method for assay of the bulk drug and finished product. From an analytical standpoint has found the application satisfactory as of 10/28/96.

STABILITY - (ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?): Accelerated (3 month) and room temperature (24 month) stability data were provided for the dry powder and reconstituted solution of each strength. The data supports the requested 24-month expiration dating period. The container/closure systems used in the stability studies were identical to those described in the container section.

LABELING: Acceptable as per A.Vezza (8/11/97)

STERILIZATION VALIDATION: Not-applicable

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?): The applicant's bio batch (#P00194; 375 mg/5 mL) was 90 kgs. The batch was manufactured with active ingredient from Ranbaxy (AADA

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?): The stability batches for each strength were kgs. They were manufactured with Ranbaxy active ingredient.

PROPOSED PRODUCTION BATCH - (MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?): The proposed production batch size is kgs. The manufacturing process described in the master production record is essentially the same as that described in the executed batch records for the bio and stability batches.

CHEMIST: Susan Rosencrance **DATE:** 7/31/97; updated 8/18/97

TEAM LEADER: John Harrison **DATE:** 8/19/97

OFFICE OF GENERIC DRUGS
CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

1. CHEMIST'S REVIEW NO. 2

2. AADA#'s 64-155, 64-164, 64-165, 64-166

3. NAME AND ADDRESS OF APPLICANT
Ranbaxy Pharmaceuticals Inc.
4600 Marriott Drive Suite 100
Raleigh, North Carolina 27612

4. LEGAL BASIS FOR AADA SUBMISSION
21 CFR §442.104b - The application is based on the RLD **Ceclor®** manufactured by Eli Lilly (AADA 62-206).

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Cefaclor for Oral Suspension USP

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES
Firm:
Original Submission (64-155): 7/7/95
Amendment (64-155): 9/27/95
Original Submission (64-164, 64-165, 64-166): 9/27/95
Amendment (major): 5/28/97

FDA:
Refusal to File: 9/20/95
Acknowledgement (64-165): 11/8/95
Acknowledgement (64-155, 64-164, 64-166): 11/17/95
Deficiency Letter: 2/7/96

10. PHARMACOLOGICAL CATEGORY
Antibacterial

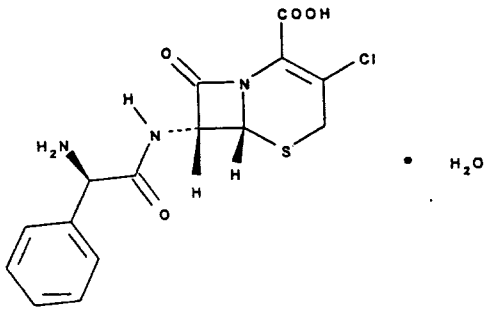
11. HOW DISPENSED
℞

12. RELATED IND/NDA/DMFs
AADA 62-206 - Eli Lilly (Listed Drug, Ceclor®)
AADA
DMF
DMF

13. **DOSAGE FORM**
Dry mixture for oral suspension.

14. **STRENGTH**
125 mg/5 mL (64-166)
187 mg/5 mL (64-165)
250 mg/5 mL (64-164)
375 mg/5 mL (64-155)

15. **CHEMICAL NAME AND STRUCTURE**



3-Chloro-7-D-(2-phenylglycinamido)-3-cephem-4-carboxylic acid monohydrate.

$C_{15}H_{14}ClN_3O_4S.H_2O$
Molecular Weight: 385.82

16. **RECORDS AND REPORTS**
N/A

17. **COMMENTS**
All deficiencies noted after Chemistry Review #1 were satisfactorily resolved in the firm's 5/28/97 amendment.

18. **CONCLUSIONS/RECOMMENDATIONS**
Approval is recommended

19. **REVIEWER**
/S/
Susan Rosencrance 8/18/97

DATE COMPLETED
7/30/97; updated 8/18/97

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Chem #2

Office of Generic Drugs
Chemistry, Manufacturing and Controls Review

1. **CHEMIST'S REVIEW NO.** 1

2. **AADA#** 64-155, 64-164, 64-165, 64-166

3. **NAME AND ADDRESS OF APPLICANT**
Ranbaxy Laboratories Limited
4600 Marriott Drive Suite 100
Raleigh, North Carolina 27612

4. **LEGAL BASIS FOR AADA SUBMISSION**
21 CFR §442.104b - The application is based on the reference drug **Ceclor®** manufactured by Eli Lilly (AADA 62-206).

5. **SUPPLEMENT(s)**
N/A

6. **PROPRIETARY NAME**
N/A

7. **NONPROPRIETARY NAME**
Cefaclor for Oral Suspension USP

8. **SUPPLEMENT(s) PROVIDE(s) FOR**
N/A

9. **AMENDMENTS AND OTHER DATES**
Firm:
Original Submission (64-155): 7/7/95
Amendment (64-155): 9/27/95
Original Submission (64-164, 64-165, 64-166): 9/27/95

FDA:
Refusal to File: 9/20/95
Acknowledgement of Receipt (64-165): 11/8/95
Acknowledgement of Receipt (64-155, 64-164, 64-166): 11/17/95

10. **PHARMACOLOGICAL CATEGORY**
Antibacterial

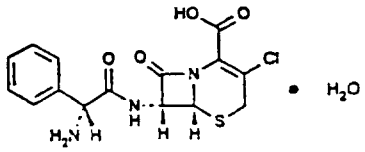
11. **HOW DISPENSED**
Rx

12. **RELATED IND/NDA/DMFs**
AADA 62-206 - Eli Lilly (Listed Drug, Ceclor®)
AADA
DMF
DMF

13. **DOSAGE FORM**
Dry mixture for oral suspension.

14. **STRENGTH**
125 mg/5 mL (64-166)
187 mg/5 mL (64-165)
250 mg/5 mL (64-164)
375 mg/5 mL (64-155)

15. **CHEMICAL NAME AND STRUCTURE**



(1) 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[(aminophenylacetyl)amino]-3-chloro-8-oxomonohydrate, [6R-[6α,7ß(R*)]]-;

(2) (6R,7R)-7-[(R)-2-Amino-2-phenylacetamido]-3-chloro-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate;

(3) 3-Chloro-7-D-(2-phenylglycinamido)-3-cephem-4-carboxylic acid monohydrate.

$C_{15}H_{14}ClN_3O_4S.H_2O$
Molecular Weight: 385.82

16. **RECORDS AND REPORTS**
N/A

17. **COMMENTS**
See review comments for deficiencies with respect to chemistry, manufacturing and control issues. Other pending issues include a review by Bioequivalence, sample analysis and an EER.

18. **CONCLUSIONS/RECOMMENDATIONS**
Not-Approvable (Major)

19. **REVIEWER**
Susan Rosencrance /S/ 2/1/96

DATE COMPLETED
1/25/96

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Chem #1